Image

DAC 1626

Atty. Dkt. No. 040283-0196

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Jonathan Richard Anthony ROFFEY et al.
Title:	CONDENSED INDOLINE DERIVATIVES AND THEIR USE AS 5HT, IN PARTICULAR 5HT2C, RECEPTOR LIGANDS
Appl. No.:	10/009,567 Filing Date: 04/05/2002
Examiner:	Rebecca L. Anderson Art Unit: 1626

PETITION AGAINST RESTRICTION REQUIREMENT

Mail Stop Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

Applicants hereby petition the Group Director of Art Unit 1600 under 37 C.F.R. §1.181 for the examination of all of the claims of the captioned application on the grounds that the claims have unity of invention. Under 37 C.F.R. §1.181(f), this petition is being filed on a timely basis, within two months of the mailing date of the Office Communication dated September 29, 2003.

Action Requested

In accordance with MPEP § 1893.03(d), Rule 13 of the PCT instructions, and 37 C.F.R § 1.475, applicants petition for the examination of all of the pending claims on the grounds that the claims have unity of invention.

Statement of Facts

1. On June 6, 2003, the Examiner issued a restriction requirement, dividing the invention into six Groups. The restriction requirement stated that the claims did not have a special technical feature that defined a contribution over the prior art. Specifically, the examiner alleged that the N-amino indoline did not define a contribution over 5,633,276.

2. Applicants filed a response to the restriction requirement on July 7, 2003, by traversing the restriction requirement, provisionally electing a species and suggesting a starting point for the examination of the claims. Applicants argued that the finding of the

lack of unity was improper because it ignored the totality of the claimed structure, which was a N-amino indoline with a branched amino ethyl group, *i.e.* a $-(CH_2)(CHR_3)_pNR_1R_2$.

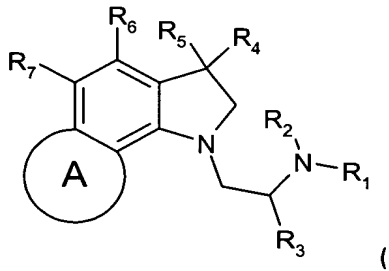
3. The Examiner issued an Office Action on the merits dated September 29, 2003. While the Examiner did expand certain aspects of the examination over the original restriction requirement, (see pages 5-6 of the Office Action), the Examiner, without elaboration, stated that the aminoethyl group $-(CH_2)(CHR_3)_pNR_1R_2$ is not considered part of the invention. (See sentence spanning pages 5-6.) The Examiner admitted at page 2 that "the variables on the N-amioethyl indoline differ from those of US '276." The Examiner also stated that even if the aminoethyl group $-(CH_2)(CHR_3)_pNR_1R_2$ were considered part of the invention, the invention would still not have a special technical feature over US 5,755,829, a newly cited patent.

Argument

Argument With Respect to the Chemical Compound

The Restriction Requirement Arbitrarily Ignores What the Applicants Define to be Their Invention

Claim 1 of the present invention is directed to the following core structure of formula (I):



(I)

R_3 is defined by the claims to be alkyl. Thus, as part of the core structure what applicant's claim to be their invention, there is a branched 2-aminoakyl group attached to the N of the tricyclic indoline.

PCT Rule 13.2

Determination of unity of invention under the Patent Cooperation Treaty is governed by PCT Rule 13.2, which defines unity of invention to exist where there is technical

relationship among the inventions involving one or more of the same or corresponding special technical features. As stated in Rule 13.2, reproduced below, special technical features are required by the Treaty to be treated as a whole.

> § 13.2 Circumstances in Which the Requirement of Unity of Invention Is to Be Considered Fulfilled
>
> Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, *considered as a whole*, makes over the prior art. (Emphasis added.)

Applicants contend that the outstanding restriction requirement does not view Formula (I) as a whole and is, therefore, improper. Properly viewed as a whole, it should be recognized that Formula (I) is a tricyclic indoline-type moiety with a branched 2-aminoakyl group attached to the N of the tricyclic indoline.

Administrative Instructions Under the PCT

The Administrative Instructions Under the PCT, Annex B, Part 1 at page AI-63 of the MPEP, provide further guidance as to the meaning of the "special technical feature" defined in Rule 13.2. The last sentence of paragraph (b) at page AI-63 states "[t]he determination [of special technical features] is made on the contents of the claims as interpreted in light of the description and drawings (if any)." The specification of the present application fully supports that the branched 2-aminoakyl group attached to the N of the tricyclic indoline is a special technical feature. See Formula I at page 5 of the present specification. Claim 1 of the present application fully supports this as well.

Examples of the Administrative Instructions Under the PCT

Applicants also contend the decision to exclude the branched 2-aminoalkyl group as part of the special technical feature is contrary to Examples 19 and 20 of the Administrative Instructions Under the PCT at pages AI 71-72 of the MPEP. Examples 19 and 20 are considered common structures where unity of invention was found. Both structures in their

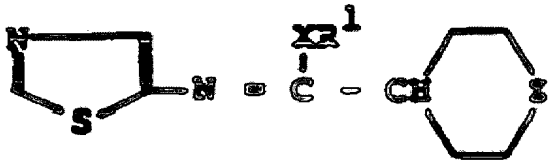
totality have a heterocyclic core linked to a linear chain, both of which were considered when evaluating the unity of invention. Examples 19 and 20 are reproduced below.

Example 19 is a compound of the formula:

wherein R_1 is selected from the group consisting of phenyl, pyridyl, thiazolyl, triazinyl, alkylthio, alkoxy, and methyl; Z is selected from the group consisting of oxygen (O), sulfur (S), imino (NH), and methylene (-CH_2-). The compounds are alleged to be useful as pharmaceuticals for relieving lower back pain.

In this particular case *the iminothioether group -N=C-SCH_3 linked to a six atom ring is the significant structural element which is shared by all the alternatives.* Thus, since all the claimed compounds are alleged to possess the same use, unity would be present. A six membered heterocyclic ring would not have been of sufficient similarity to allow a Markush grouping exhibiting unity, absent some teaching of equivalence in the prior art. (Emphasis added.)

Example 20



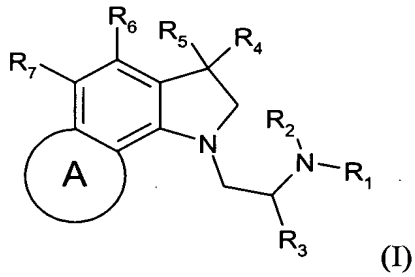
wherein R^1 is methyl or phenyl, X and Z are selected from oxygen (O) and sulfur (S).

The compounds are useful as pharmaceuticals and contain the 1,3-thiazolyl substituent which provides greater penetrability of mammalian tissue which fact

makes the compounds useful as relievers for headaches and as topical anti-inflammatory agents.

All compounds share a common chemical structure, the thiazole ring and the six atom heterocyclic compound bound to an imino group, which occupy a large portion of their structure. A six membered heterocyclic ring would not have been of sufficient similarity to allow a Markush grouping exhibiting unity, absent some teaching of equivalence in the prior art. (Emphasis added.)

In both Examples 19 and 20 of the Administrative Instructions Under the PCT, the entire chemical structure, common to all chemical compounds, was found to posses unity of invention. In the present claims, the structure common to all chemical compounds is the structure of Formula (I) as depicted below.



(I)

wherein: R_1 and R_2 are independently selected from hydrogen and alkyl; R_3 is alkyl; R_4 and R_5 are selected from hydrogen and alkyl; R_6 and R_7 are independently selected from hydrogen, halogen, hydroxy, alkyl, aryl, amino, alkylamino, dialkylamino, alkoxy, aryloxy, alkylthio, alkylsulfoxyl, alkylsulfonyl, nitro, carbonitrile, carbo-alkoxy, carbo-aryloxy and carboxyl; and A is a 5- or 6-membered ring optionally containing one or more heteroatoms wherein the atoms of the ring A, other than the unsaturated carbon atoms of the phenyl ring to which the ring A is fused, are saturated or unsaturated, or a pharmaceutically acceptable salt, addition compound or prodrug thereof.

In conclusion, the decision to not consider the branched 2-aminoakyl group along with the rest of the structure of Formula I which is common to all claims is not supportable under PCT Rule 13, the Administrative Instructions Under the PCT, and the examples under the Administrative Instructions.

The Combination of U.S. Patent No. 5,633,276 and 5,755,829 Does Not Support a Finding of a Lack of Unity of Invention

The Examiner first cited Formula I U.S. Patent No. 5,633,276 to support a finding of lack of unity of invention. See pages 4-5 of the Office Action dated June 6, 2003. Although the Examiner claimed to analyze the present invention as a whole, in the written Office Action, the Examiner's analysis did not take into account the invention includes a branched amino ethyl group, *i.e.* a $(CH_2)(CHR_3)_pNR_1R_2$. In a subsequent telephone conversation with the undersigned representative of the Applicants, the Examiner stated that the branched amino ethyl group was not part of the invention's "core" and therefore would not be considered for purposes of unity of invention.

In the next Office Action, the Examiner stated that even if the $(CH_2)(CHR_3)_pNR_1R_2$ moiety were considered to be part of the invention, there would still be no unity of invention over the structure disclosed at column 2, lines 5-51 U.S. Patent No. 5,755,829 (apparently in combination with Formula I of U.S. Patent No. 5,633,276.) Applicants contend that the '829 patent does not cure the deficiencies of the '276 patent. The '829 patent discloses a bicyclic indoline compound that is used in a dyeing process and is not described as having any pharmaceutical properties. Moreover, there is no suggestion to select the $(CH_2)(CHR_3)_pNR_1R_2$ moiety from the vast array of possible substituents of the R_1 variables disclosed at column 2, lines 14-29 of the '829 patent. In contrast to the '829 patent, the present invention is tricyclic and has a $(CH_2)(CHR_3)_pNR_1R_2$. None of these aspects of the present invention are taught or suggested by the '829. Finally, due to very different structures and uses of the '829 and '276 patents, applicants contend that there would be no motivation to combine these two references to arrive at the present invention.

Argument with Respect to the Method

Applicants urge that all of the pending method claims have unity of invention because they are linked by a common structure. Moreover, the specification supports the proposition that the pending method claims have unity of invention. The Examiner has provided no evidence to the contrary. Finally, the references submitted with the July 7, 2003 response support applicants' position with respect to the unity of invention with the method of use claims. For example, the article *Curr. Opin. Invest. Drugs* by Kennet, discusses how the

present invention might be useful with respect to "cognitive impairment" (pages 340-341), "migraine prophylactic properties" (page 343), or "intracranial pressure [from] mass lesions, head trauma, acute or hydrocephalus, or pseudotumor cerebi" (pages 344-345).

Therefore, examination on the merits with respect to all of the pending claims is respectfully requested. Should the Office fail to find unity of invention with respect to claim 1, at the very least, the Office is respectfully requested to find unity of invention with respect to one or more of new claims 31-36, in particular claims 31-34, most preferably claim 31. All of these claims represent sub genera of claim 1, but allow for more variation of the A ring than the outstanding restriction requirement.

Should additional fees be necessary in connection with the filing of this response, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

Respectfully submitted,

Date December 1, 2003

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